

**ATTACHMENT A**  
**Remarks**

Claims 3-6 are pending in the present application. By this Amendment, Applicants have added new claims 5 and 6. Applicants respectfully submit that the present application is in condition for allowance based on the discuss which follows.

In the outstanding final Office Action, claims 3 and 4 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nyamekye et al. (Circulation 1995; 91:417-425) (hereinafter "Nyamekye") in view of Narciso, Jr. (U.S. Patent No. 5,298,018) (hereinafter "Narciso") and Aizaw et al. (U.S. Patent No. 5,308,861 (hereinafter "Aizaw"). With regard to Narciso, the Examiner maintains that Narciso teaches photodynamic therapy ("PDT") during PTCA to limit restenosis of a blood vessel and alleges that "since Narciso teaches the use of photodynamic therapy during a PTCA procedure, all method steps of the instant claims are also inherently disclosed." Further, the Examiner alleges that since Narciso discloses the use of a laser at a dose of 20 J/cm<sup>2</sup>, it would be obvious to use the claimed lower power of 1-10 J/cm<sup>2</sup>.

Contrary to the rejection of the claims, the present invention is not obvious over the prior art of record. The present invention is directed to laser irradiating using an optical fiber balloon catheter within a vascular lumen of a blood vessel at the angioplasty-injured site, which obtains an even or uniform and sufficient laser irradiation, which is applied to the intravascular blood vessel inner wall to irradiate a photosensitizing compound present in the blood vessel wall at the angioplasty-injured site, so that restenosis is inhibited successfully and to its full extent.

Distinguishing features of the present invention were presented in the Remarks to the Amendment filed September 5, 2006, which includes:

1. preventing restenosis following a PTCA procedure;
2. specifically locating a balloon catheter at the angioplasty-dilated and injured site during the PDT procedure;
3. timing the PDT treatment 0.5-6 hours after administering a single treatment of a photosensitizing compound; and
4. using a relatively lower laser fluence of  $1-10 \text{ J/cm}^2$  in a method of preventing of restenosis.

In sharp contrast to the present method, Narciso teaches the use of PDT following PTCA to lyse plaques and lesions and SMC cells which uses:

1. multiple readministrations of a photosensitizing compound;
2. a relatively higher laser fluence power of  $20 \text{ J/cm}^2$ ; and
3. fails to teach the use of an inflated balloon catheter at an angioplasty-dilated and injured site to completely occlude the blood flow in a treatment to lyse arteriosclerotic lesions or plaques, as well as SCM cells (see, e.g., Remarks, September 5, 2006 Amendment, pages 1-10).

Furthermore, contrary to the Examiner's remark in the Response to Arguments section of the November 30, 2006 Office Action that "optimizing the laser wavelengths and density is a matter of routine experimentation," procedural differences between the claimed method and Narciso with regard to blood occlusion, photosensitizing compound administration, and other processing conditions fail to make the claimed laser wavelength and intensity obvious as a matter of routine experimentation. Narciso

teaches multiple administrations of a photosensitizing compound over the course of 5-18 days, followed by irradiation at 20 J/cm<sup>2</sup>. Nowhere does Narciso suggest one could use one-half the power with its procedure.

In response to the Examiner's statement that the claimed single administration of a photosensitizing compound is anticipated by Narciso, which teaches multiple doses, alleging that the term "comprising" renders the claim open, Applicants respectfully submit that the claimed single administration of a photosensitizing compound is a specific limitation which is not rendered obvious by Narciso. Although claim 3 uses the transitional phrase "comprising," the single administration limitation is in no way taught or suggested by a reference which teaches multiple administration sessions of a photosensitizing compound.

Thus, the present invention is further distinguishable from Narciso which fails to teach or suggest the use of a PDT procedure during the PTCA procedure. Based on the foregoing, Applicants respectfully request that the rejection to claims 3 and 4 under 35 U.S.C. § 103(a) be withdrawn.

Further, by this Amendment, Applicant has added new claims 5 and 6, specifically directed to additional features disclosed, but previously not claimed, which further distinguish the claimed method from the prior art, including Narciso and Nyamekye. By this Amendment, Applicants have added new claim 5, which corresponds to claim 3, with the additional limitation of affirmatively reciting achieving a necessary centering of a laser irradiating optical fiber within a vascular lumen of a blood vessel by using a completely inflated balloon catheter. Further, as recited in new claim 5, the completely inflated balloon completely intercepts the bloodstream flow while

resulting in and enabling that any blood flow that has been blocked from flowing between the completely inflated balloon wall and the blood vessel at the angioplasty-dilated and injured site does not interfere with or attenuate an irradiating laser light which is to be emitted from the optical fiber during photodynamic therapy. Accordingly, claim 5 is further distinguishable over the prior art, including art cited in the outstanding Office Action, which fails to teach or suggest totally intercepting the blood flow during a PDT procedure using a balloon catheter which centers and maintains proper alignment, i.e. continuous centering of the laser emitting optical fiber.

In sharp contrast to the present method, in the prior art, including art cited in the outstanding Office Action, during prior known PDT procedures which use a simple-structure, laser-irradiating, cylindrical optical fiber, complete and steady suppression of restenosis cannot be achieved with success (see present specification, page 8). As long as cylindrical optical fibers are employed for intravascular laser irradiation of an angioplasty-injured site, it is difficult to achieve a necessary centering of the cylindrical optical fiber within the vascular lumen of the blood vessel and, in particular, it is difficult to locate and maintain the longitudinal axis of the cylindrical optical fiber coincidentally with the central axis of the vascular lumen, because the bloodstream flowing around the cylindrical optical fiber moves the optical fiber and continuously changes the position of the optical fiber within the vascular lumen during the intravascular laser irradiation.

It is necessary to have constant centering of the laser irradiating cylindrical optical fiber in order to ensure that the transmission of irradiating laser emitted from the cylindrical optical fiber will not be varied, interfered with or attenuated by bloodstream flowing around the optical fiber within the vascular lumen. Moreover, without having

constant centering of a cylindrical optical fiber, the restenosis-inhibiting therapeutic effects of a photoactivated photosensitizing compound present in the blood vessel can be greatly varied and become too insufficient to achieve a consistent, successful inhibition of restenosis, as desired. For a more complete discussion, please see the present specification, page 16, line 15 to page 19, line 6.

Accordingly, the present method overcomes previously known problems in the prior art by using a fully inflated laser irradiating optical fiber balloon catheter which results in a constant centering of the fiber within the vascular lumen of the blood vessel at the angioplasty-injured site to thereby obtain an even or uniform and sufficient laser irradiation, which is applied to the intravascular blood vessel inner wall, and to irradiate the photosensitizing compound present in the blood vessel wall at the angioplasty-injured site so that restenosis is inhibited successfully and to its full extent. The necessary and constant centering of the laser irradiating optical fiber within the vascular lumen is achieved successfully using the present method via a completely inflated balloon catheter of the device during the PDT procedure, where the bloodstream is intercepted completely due to the completely inflated balloon.

Turning now to the prior art which was the subject of the outstanding Office Action, Narciso fails to disclose a desire to center the laser irradiating optical fiber, let alone a constant centering of the optical fiber which is inserted into the intravascular lumen. Further, Narciso fails to teach or suggest how to center a laser irradiating optical fiber or how to achieve uniform laser irradiating using a cylindrical optical fiber if the optical fiber is not properly aligned within the intravascular lumen.

Furthermore, Narciso clearly discloses in column 9, lines 18-33, using a 1.5 mm catheter with a 2 cm tip, where the catheter diameter creates an annulus of blood flow around the catheter with a thickness of 0.25 mm. Further, Narciso discloses a blood attenuation of 50% of the light power in a 0.25 mm thickness of blood flow around the catheter so that with a total delivery dose of light of  $20 \text{ J/cm}^2$ , a total time for the PDT procedure is 50 seconds. Therefore, Narciso fails to teach or suggest complete interception of bloodstream around an intravascularly inserted catheter during the PDT procedure.

It would not have been obvious for one of ordinary skill in the art to fully occlude a blood vessel using a fully inflated balloon catheter, as the prior art clearly teaches away from such a procedure. Previously cited Honye et al. teaches that the angioplasty-dilated site is subject to dissection, tearing and rupture (see Remarks, page 3, first complete paragraph). Further, U.S. Patent No. 5,766,584 to Edelman et al. (hereinafter "Edelman"), column 1, lines 44-51 discloses that when a balloon that is intravascularly inserted is overinflated, a variety of undesirable results occur, such as rupture of the tunica intima of the blood vessel. Therefore, one of ordinary skill in the art would not be motivated to use a completely inflated balloon and, in fact, would be taught away from using a completely inflated balloon during the PDT procedure in a post-angioplasty treatment. Therefore, contrary to the Examiner's assertion, it would not have been obvious to use a fully inflated balloon which fully occludes a blood vessel.

In complete contrast to the teachings of Honye and Edelman, in the present method, a portion or region of the blood vessel at the angioplasty-injured site is kept in tight contact with a completely inflated balloon, which has been inserted within the

vascular lumen, resulting in the lumen being distended. Further, the vascular lumen is distended when being irradiated using laser light during the PDT procedure, which results in obtaining the effect of increasing the cross-sectional area of the vascular lumen as previously discussed on page 7, in the third complete paragraph to page 8, first complete paragraph of the Remarks section of the September 5, 2006 Amendment. Accordingly, the present procedure is completely unpredictable and non-obvious in view of the disclosure of Narciso.

With regard to Nyamekye, this reference teaches that when the PDT procedure, using the ALA-PPIX sensitizer, is applied at the same time as the angioplasty, the experimental intimal hyperplasia development, namely the restenosis in the blood vessel, can be inhibited in rats.

Finally, further in response to the Examiner's statement that a claim using the transitional phrase "comprising" and reciting a single administration of a photosensitizing compound is anticipated by Narciso, which teaches multiple doses, notwithstanding the argument made above with regard to this rejection applied to claim 3, and in order to eliminate any doubt, new claim 5 uses the transitional phrase "consisting of" to further emphasize that the claimed single photosensitizing compound administration is distinguishable from Narciso, which teaches multiple administrations.

Based on the individual and divergent teachings of the prior art, one of ordinary skill in the art would not be motivated to develop a method which makes claims 5 and 6 obvious. Based on the foregoing, Applicants respectfully submit that claims 5 and 6 are not obvious in view of the prior art of record.

In view of the foregoing, Applicants respectfully submit that the present application is in condition for allowance.

**END REMARKS**